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EXAMINER	
CHAKRABARTI, ARUN K	

ART UNIT	PAPER NUMBER
1634	

DATE MAILED: 10/08/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary

Application No.	Applicant(s)
09/868,043	Caillat
Examiner	**Art Unit**
Arun Chakrabarti	1634

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136 (a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1) ☒ Responsive to communication(s) filed on *Aug 11, 2003* .

2a) ☐ This action is **FINAL**. 2b) ☒ This action is non-final.

3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11; 453 O.G. 213.

Disposition of Claims

4) ☒ Claim(s) *27-54* is/are pending in the application.

4a) Of the above, claim(s) _____ is/are withdrawn from consideration.

5) ☐ Claim(s) _____ is/are allowed.

6) ☒ Claim(s) *27-54* is/are rejected.

7) ☐ Claim(s) _____ is/are objected to.

8) ☐ Claims _____ are subject to restriction and/or election requirement.

Application Papers

9) ☐ The specification is objected to by the Examiner.

10) ☐ The drawing(s) filed on _____ is/are a) ☐ accepted or b) ☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11) ☐ The proposed drawing correction filed on _____ is: a) ☐ approved b) ☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12) ☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13) ☐ Acknowledgement is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a) ☐ All b) ☐ Some* c) ☐ None of:

1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. _____ .
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

*See the attached detailed Office action for a list of the certified copies not received.

14) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. § 119(e).

a) ☐ The translation of the foreign language provisional application has been received.

15) ☐ Acknowledgement is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s). _____
4) ☐ Interview Summary (PTO-413) Paper No(s). _____
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☒ Other: *Detailed Action*

DETAILED ACTION

Continued Examination Under 37 CFR 1.114

1. A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on August 11, 2003 has been entered.

Specification

2. Claims 27, 37, and 49 have been amended.Claim 54 has been represented (formerly dependent claim 43(2)).

Claim Rejections - 35 USC § 102

3. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

4. Claims 27, 29, and 37are rejected under 35 U.S.C. 102(b) as being anticipated by Muller et al. (U.S. Patent 5,151,162) (September 29, 1992).

Muller et al. teach a method to produce a blank biochip (Abstract), comprising:

a) providing a substrate;

b) depositing a layer of material on the substrate; wherein the layer initiate and promote the adhesion of a copolymer film comprising a pyrrole and a functionalized pyrrole by electropolymerisation;

c) coating the layer of material with a resin layer (Column 5, lines 16-42),

d) producing a plurality of microtroughs inherently in the resin layer wherein the layer of materials forms at least a part of the base of the microtroughs (Column 5, lines 16-42 and Example 1) (this inherency is deduced from the fact that resin layers are unevenly spread always naturally forming microtroughs naturally), and further comprising

Muller et al teach a method, wherein the layer of material capable of initiating and promoting the adhesion of the polypyrrole film by electropolymerisation being a metallic layer of gold, step a) comprises a deposition step of the metallic layer onto the substrate, and a deposition step of a layer of resin or polymer onto the metallic layer and engraving of the resin layer so as to form microtroughs, wherein the base is composed at least partly of the metallic layer (Column 5, lines16-42).

Claim Rejections - 35 USC § 103

5. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was

commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

6. Claims 28-31, 38-40, 42-43, 45, 46, and 50-54 are rejected under 35 U.s.C. 103(a) over Muller et al. (U.S. Patent 5,151,162) (September 29, 1992) in view of Teoule et al. (U.S. Patent 5,837,859) (November 17, 1998).

Muller et al teach a method of claims 27, 29, and 37 as described above.

Muller et al does not teach a method of directly or indirectly fixating a biological probe to the functioinalized pyrrole, by injecting a biological probe solution, in one or more microtroughs in the presence of chemical reagents required for the fixation.

Teoule et al teach a method of directly or indirectly fixating a biological probe to the functioinalized pyrrole, by injecting a biological probe solution, in one or more microtroughs in the presence of chemical reagents required for the fixation (Examples 1-5).

Muller et al does not teach a method, wherein step a) also comprises a chemical treatment step of the gold layer at the base of the microtoughs in the presence of a functionalized pyrrole for example with a thiol group so as to form a monolayer of pyrrole onto the gold layer, at the base of the microtoughs

Teoule et al teach a method, wherein step a) also comprises a chemical treatment step of the gold layer at the base of the microtoughs in the presence of a functionalized pyrrole for

example with a thiol group so as to form a monolayer of pyrrole onto the gold layer, at the base of the microtoughs (Examples 6-7).

Muller et al does not teach a method, wherein the collective electropolymerisation is carried out by immersing the structured substrate obtained in step a) in an electrolytic bath comprising a solution of pyrrole, functionalized pyrrole, and suitable chemical reagents for electropolymerisation, in the presence of a counterelectrode which is immersed in the electrolytic bath and is independent of the structured substrate, the layer of material capable of initiating and promoting the adhesion onto the layer of the pyrrole and functionalized pyrrole copolymer film forming a working electrode.

Teoule et al teach a method, wherein the collective electropolymerisation is carried out by immersing the structured substrate obtained in step a) in an electrolytic bath comprising a solution of pyrrole, functionalized pyrrole, and suitable chemical reagents for electropolymerisation, in the presence of a counterelectrode which is immersed in the electrolytic bath and is independent of the structured substrate, the layer of material capable of initiating and promoting the adhesion onto the layer of the pyrrole and functionalized pyrrole copolymer film forming a working electrode (Example 2- Principle of the technique and Method Section).

Muller et al does not teach a method, wherein the functionalized pyrrole is a pyrrole comprising a group chosen in a set comprising an NH2 group (aminoethyl pyrrole in this case).

Teoule et al teach a method, wherein the functionalized pyrrole is a pyrrole comprising a group chosen in a set comprising an NH2 group (aminoethyl pyrrole in this case) (Example 4 and Figures 7-8).

Muller et al does not teach a method, wherein the fixation of the biological probe being indirect, the method also comprises, in step c) before the fixation of the biological probe, a collective fixation of a cross-linking agent on the functionalized pyrrole, in the presence of suitable chemical reagents, the cross-linking agent comprising a first function enabling its fixation onto the functionalized pyrrole, and a second function enabling the fixation of the biological probe on the cross-linking agent.

Teoule et al teach a method, wherein the fixation of the biological probe being indirect, the method also comprises, in step c) before the fixation of the biological probe, a collective fixation of a cross-linking agent on the functionalized pyrrole, in the presence of suitable chemical reagents, the cross-linking agent comprising a first function enabling its fixation onto the functionalized pyrrole, and a second function enabling the fixation of the biological probe on the cross-linking agent (Example 4).

Muller et al does not teach a method, wherein the cross-linking agent is chosen from a diacid.

Teoule et al teach a method, wherein the cross-linking agent is chosen from a diacid (dichloromethane in this case) (Examples 4 and 7).

Muller et al does not teach a method, wherein the biological probe is a functionalized oligonucleotide to be fixed either directly or indirectly onto a functionalized pyrrole.

Teoule et al teach a method, wherein the biological probe is a functionalized oligonucleotide to be fixed either directly or indirectly onto a functionalized pyrrole (Examples 1-5).

Muller et al does not teach a biochip comprising

- an oligonucleotide fixed directly on the functionalized pyrrole, or indirectly on the functionalized pyrrole by means of the crosslinking agent bound to the pyrrole

Teoule et al teach a biochip comprising

- an oligonucleotide fixed directly on the functionalized pyrrole, or indirectly on the functionalized pyrrole by means of the crosslinking agent bound to the pyrrole (Column 5, line 64 to column 6, line 24).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a biochip comprising

- an oligonucleotide fixed directly on the functionalized pyrrole, or indirectly on the functionalized pyrrole by means of the crosslinking agent bound to the pyrrole of Teoule et al. in the method of Muller et al., since Teoule et al. state, "The aim of the present invention is to obtain novel supports and novel processes for binding oligonucleotides, which do not have the drawbacks of the processes proposed in the prior art. The inventors are now able to bind stably, and via a covalent bond, nucleotides and oligonucleotides to an electrically conductive polymer, and thereby to obtain novel copolymers (Column 1, lines 58-67)." An ordinary practitioner would have been motivated to combine and substitute a biochip comprising

- an oligonucleotide fixed directly on the functionalized pyrrole, or indirectly on the functionalized pyrrole by means of the crosslinking agent bound to the pyrrole of Teoule et al. in the method of Muller et al., in order to achieve the express advantages noted by Teoule et al., of a novel invention which provides novel supports and novel processes for binding oligonucleotides,

which do not have the drawbacks of the processes proposed in the prior art and by which the inventors are now able to bind stably, and via a covalent bond, nucleotides and oligonucleotides to an electrically conductive polymer, and thereby to obtain novel copolymers.

7. Claims 32-34 and 47-49 are rejected under 35 U.S.C. 103(a) over Muller et al. (U.S. Patent 5,151,162) (September 29, 1992) in view of Teoule et al. (U.S. Patent 5,837,859) (November 17, 1998) further in view of Livache et al. (Nucleic Acids Research, (1994), Vol. 22 (15), pages 2915-2921).

Muller et al. in view of Teoule et al. teach the method of claims 28-31, 38-40, 42-43, 45, 46, and 50-52 as described above. Muller et al also teaches the method of claim 49 of immersing the structured substrate in an electrolyte bath comprising a solution of pyrrole, and suitable chemical reagents for electropolymerisation, in the presence of a counterelectrode which is immersed in the electrolyte bath and is independent of the structural substrate, wherein the layer of material forms a working electrode (Figure 1).

Muller et al. in view of Teoule et al do not teach the method, wherein functionalized pyrrole with a thiol group has the formula of claim 6, wherein n has a value ranging from 2 to 10.

Livache et al. teach the method, wherein functionalized pyrrole with a thiol group has the formula of claim 6, wherein n has a value equal to 1 (MATERIALS and METHODS Section, Synthesis of pyrrole modified phosphoramidite Subsection).

"Compounds which are position isomers (compounds having the same radicals in physically different positions on the same molecules) or homologs (compounds differing regularly

by the successive addition of the same chemical group, e.g., by -CH 2- groups) are generally of sufficient close structural similarity that there is a presumed expectation that such compounds possess similar properties. *In re wilder,* 563 F.2D 457, 195 USPQ 426 (CCPA 1977). See also *In re May,* 574 F.2d 1082, 197 USPQ 601 (CCPA 1978) (stereoisomers *prima facie* obvious)." (See MPEP 2144.09, Paragraph II).

Therefore, the organic spacer group, the methylene group which is located between the pyrrole ring and the SH group comprising (CH 2)n, wherein n is equal to 2-10 , is functionally equivalent to the compounds taught by Livache et al. It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a method, wherein the organic spacer group, the methylene group which is located between the pyrrole ring and the SH group comprising (CH 2)n, wherein n is equal to 2-10 , which is functionally equivalent to the compounds taught by Livache et al. in the method of Muller et al. in view of Teoule et al., since Livache et al. state, "Covalent linkage can be obtained by polymerization of modified pyrrole; thus small molecules have been immobilized by this method in polypyrrole films for electrochemical studies (Page 2915, Column 2, lines 11-13)." An ordinary practitioner would have been motivated to combine and substitute a method, wherein the organic spacer group, the methylene group which is located between the pyrrole ring and the SH group comprising (CH 2)n, wherein n is equal to 2-10 , which is functionally equivalent to the compounds taught by Livache et al. in the method of Muller et al. in view of Teoule et al. in order to achieve the express advantages noted by Livache et al. of a method , which provides covalent linkage that can be obtained by polymerization of

modified pyrrole; thus immobilizing small molecules in polypyrrole films for electrochemical studies.

8. Claims 35-36 are rejected under 35 U.S.C. 103(a) over Muller et al. (U.S. Patent 5,151,162) (September 29, 1992) in view of Simon et al. (Journal of American Chemical Society, (1982), Vol. 104, pages 2031-2034).

Muller et al. teach the method of claims 27, 29, and 37 as described above.

Muller et al. do not teach the method, wherein the sialanisation agent is N-(3-(trimethoxy silyl) propyl) pyrrole.

Simon et al. teach the method, wherein the sialanisation agent is N-(3-(trimethoxy silyl) propyl) pyrrole. (Page 2031, last 10 lines).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a method, wherein the sialanisation agent is N-(3-(trimethoxy silyl) propyl) pyrrole as taught by Simon et al. in the method of Muller et al., since Simon et al. state, "We now report the synthesis, characterization, and application of N-(3-(trimethoxy silyl) propyl) pyrrole, I, as a photoanode deactivating reagent that can be covalently anchored to the electrode via reaction of surface OH groups. The pendant pyrrole functionality can then be used as the initiation site for polymerization of pyrrole, thereby serving to covalently anchor the polypyrrole (Page 2031, last 10 lines)." An ordinary practitioner would have been motivated to combine and substitute a method, wherein the sialanisation agent is N-(3-(trimethoxy silyl) propyl) pyrrole as taught by Simon et al. in the method of Muller et al. in order to achieve the express advantages noted by Simon et al. of application of N-(3-(trimethoxy silyl) propyl) pyrrole, I, as a photoanode

deactivating reagent that can be covalently anchored to the electrode via reaction of surface OH groups, which in turn can then be used as the initiation site for polymerization of pyrrole, thereby serving to covalently anchor the polypyrrole.

9. Claim 41 is rejected under 35 U.S.C. 103(a) over Muller et al. (U.S. Patent 5,151,162) (September 29, 1992) in view of Teoule et al. (U.S. Patent 5,837,859) (November 17, 1998) further in view of Lizardi et al. (U.S. Patent 6,316,229 B1) (November 13, 2001).

Muller et al. in view of Teoule et al teach the method of claims 27-31, 37-40, 42-43, 45, 46, and 50-52 as described above.

Muller et al. in view of Teoule et al do not teach the method, wherein the cross-linking agent is glutaraldehyde.

Lizardi et al. teach the method, wherein the cross-linking agent is glutaraldehyde (Column 33, line 66 to column 34, line 20).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute a cross-linking agent glutaraldehyde as taught by Lizardi et al. in the method of Muller et al. in view of Teoule et al., since Lizardi et al. state, "A preferred attachment agent is glutaraldehyde (Column 33, line 66)." Lizardi et al further provide motivation as Lizardi et al. state,"For example, antibodies may be chemically cross-linked to a substrate that contains free amino or carboxyl groups using glutaraldehyde or carbodiimides as cross-linker agents (Column 34, lines 10-13)". An ordinary practitioner would have been motivated to combine and substitute a cross-linking agent glutaraldehyde as taught by Lizardi et al. in the method of Muller et al. in view of Teoule et al., in order to achieve the express advantages noted by Lizardi et al. of

preferred attachment agent glutaraldehyde, which provides chemical cross-linking of an antibody to a substrate that contains free amino or carboxyl groups.

10. Claim 44 is rejected under 35 U.S.C. 103(a) over Muller et al. (U.S. Patent 5,151,162) (September 29, 1992) in view of Teoule et al. (U.S. Patent 5,837,859) (November 17, 1998) in view of Heroux et al. (U.S. Patent 6,312,896 B1) (November 6, 2001).

Muller et al. in view of Teoule et al teach the method of claims 27-31, 37-40, 42-43, 45, 46, and 50-52 as described above.

Muller et al. in view of Teoule et al do not teach the method, wherein the oligonucleotide is functionalized with a thiol group.

Heroux et al. teach the method, wherein the oligonucleotide is functionalized with a thiol group (Column 12, lines 33-65).

It would have been *prima facie* obvious to an ordinary practitioner to combine and substitute the oligonucleotide functionalized with a thiol group as taught by Heroux et al. in the method of Muller et al. in view of Teoule et al., since Heroux et al. state, "By using standard coupling chemistries known in the art, it is possible to conveniently label/immobilize the natural substrate of an enzyme (the cost, labor, and uncertainty of using unnatural or synthetic substrates can be avoided). Control over the sites of labeling/immobilization can be achieved by using coupling chemistries specific for a particular functionality on a substrate (e.g., an oligonucleotide that is 5'-modified with an amino group and 3'-modified with a thiol group can be specifically labeled at the 5'-positions with the NHS ester of biotin, and specifically labeled at the 3' position with a maleimide derivative of Ru Bpy (Column 12, lines 54-65)." An ordinary practitioner

would have been motivated to combine and substitute the oligonucleotide functionalized with a thiol group as taught by Heroux et al. in the method of Muller et al. in view of Teoule et al., in order to achieve the express advantages noted by Heroux et al. of gaining control over the sites of labeling/immobilization by using coupling chemistries specific for a particular functionality on a substrate and avoiding the cost, labor, and uncertainty of using unnatural or synthetic substrates.

Response to Amendment

11. In response to amendment, all previous rejections are hereby withdrawn. However, new 102(b and 103(a) rejections have been included.

Response to Arguments

12. Applicant's arguments with respect to all pending claims have been considered but are moot in view of the new ground(s) of rejection.

Conclusion

13. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Arun Chakrabarti, Ph.D. whose telephone number is (703) 306-5818.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Gary Benzion, can be reached on (703) 308-1119. The fax phone number for this Group is (703) 305-7401.

Any inquiry of a general nature or relating to the status of this application or proceeding

should be directed to the Group analyst Chantae Dessau, whose telephone number is (703) 605-1237.

Arun Kr. Chakrabarti

ARUN K. CHAKRABARTI
PATENT EXAMINER

Arun Chakrabarti,

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September 29, 2003

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